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BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,492	MEINKE ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-60* is/are pending in the application.

4a) Of the above claim(s) *51,52 and 55-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-50,53 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to restriction requirement filed on 6/7/07 is acknowledged.

Election/Restriction

2. In response to the restriction requirement, Applicants elected, without traverse, to prosecute the Group I invention, as exemplified by claims 38-54, drawn to a hyper-immune serum reactive antigen and a pharmaceutical composition with respect to SEQ ID NO:32 and), a peptide containing at least two LysLeuLys motif.

Status of claims

3. Claims 1-37 are cancelled.

Claims 38-60 are pending.

Claims 51-52 are withdrawn from the elected group I invention, as they are not drawn to the elected immunostimulatory substance, a peptide containing at least two Lys-Leu-Lys motifs.

Therefore, claims 38-50, 53 and 54 with respect to SEQ.ID.NO:32 and immunostimulatory substance, a peptide containing at least two Lys-Leu-Lys motifs are under examination . Applicant is advised to limit the claims to the elected invention, SEQ.ID.NO. 32

Claims 55-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group of inventions M.P.E.P § 821.03.

Information Disclosure Statement

4. The Information Disclosure Statement filed on 1/29/07 is signed and a copy of the same is attached with this office action.

Claim Rejections - 35 USC 101

5. 35 U.S.C. 101 reads as Follows

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

6. Claims 38-48 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The product, hyperimmune serum reactive hyper immune serum reactive antigen as claimed, has the same characteristics as that found in nature because the protein can be obtained from *Streptococcus epidermidis* infected human body etc.

To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations which would distinguish the characteristics and utility of applicant's product as enabled in the specification from the utility of the product as it exists in nature. It is further suggested that such limitation include the terminology " purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source which imparts a distinct utility to the claimed product. For relevant case law see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim Rejections - 35 USC 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 38-50, 53 and 54 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the revised guidelines on written description available at www.uspto.gov (O.G. published January 30, 2001). This is a written description rejection.

Claims 38-50, 53 and 54 are drawn to a hyperimmune serum-reactive S.epidermidis hyper immune serum reactive antigen and pharmaceutical composition comprising an amino acid sequence of SEQ.ID.NO:32 or fragments thereof, said hyper immune serum reactive antigen or fragment comprising at least 6 or 8 or 10 contiguous amino acids of SEQ.ID.NO:32, said hyper immune serum reactive antigen or fragment comprising an amino acid sequence of 6-28, 54-59, 135-147, 193-205, 274-279, 284-291,298-308, 342-347, 360-366, 380-386, 408-425, 437-446, 457-464, 467-477, 504-510, 517-530, 535-543, 547-553, 562-569, 573-579, 592-600, 602-613, 626-631, 638-668 and/or 396-449 of SEQ ID NO: 32 , said pharmaceutical composition comprising t least one hyper immune serum reactive antigen or fragment and optionally a pharmaceutically-acceptable carrier or excipient, said composition further comprising an immunostimulatory substance, wherein the immunostimulatory substance is a

peptide containing at least two Lys-Leu-Lys motifs and said pharmaceutical composition is a vaccine.

The written description rejection is made because the claims are interpreted as drawn to a genus of variety of fragments, for example, Skeiky et al disclose fragments from *P. acnes* as shown below, having no function . Thus the art t describes no structural features common to the members of the genus, which features constitute a substantial portion of the genus.

```
ID   AAU58435 standard; protein; 140 AA.
XX
AC   AAU58435;
XX
DT   27-FEB-2002  (first entry)
XX
DE   Propionibacterium acnes immunogenic protein #19331.
XX
KW   SAPHO syndrome; synovitis; acne; pustulosis; hypertosis; osteomyelitis;
KW   uveitis; endophthalmitis; bone; joint; central nervous system; ELISA;
KW   inflammatory lesion; acne vulgaris; enzyme linked immunosorbent assay;
KW   dermatological; osteopathic; neuroprotectant.
XX
OS   Propionibacterium acnes.
XX
PN   WO200181581-A2.
XX
PD   01-NOV-2001.
XX
PF   20-APR-2001; 2001WO-US012865.
XX
PR   21-APR-2000; 2000US-0199047P.
PR   02-JUN-2000; 2000US-0208841P.
PR   07-JUL-2000; 2000US-0216747P.
XX
PA   (CORI-) CORIXA CORP.
XX
PI   Skeiky YAW,  Persing DH,  Mitcham JL,  Wang SS,  Bhatia A;
PI   L'maisonneuve J,  Zhang Y,  Jen S,  Carter D;
XX
DR   WPI; 2001-616774/71.
DR   N-PSDB; AAS59591.
XX
PT   Propionibacterium acnes polypeptides and nucleic acids useful for
PT   vaccinating against and diagnosing infections, especially useful for
PT   treating acne vulgaris.
XX
PS   Example 1; SEQ ID NO 19630; 1069pp; English.
XX
CC   Sequences AAU39105-AAU68017 represent Propionibacterium acnes immunogenic
CC   polypeptides. The proteins and their associated DNA sequences are used in
CC   the treatment, prevention and diagnosis of medical conditions caused by
CC   P. acnes. The disorders include SAPHO syndrome (synovitis, acne,
CC   pustulosis, hypertosis and osteomyelitis), uveitis and endophthalmitis.
CC   P. acnes is also involved in infections of bone, joints and the central
CC   nervous system, however it is particularly involved in the inflammatory
CC   lesions associated with acne vulgaris. A method for detecting the
CC   presence or absence of P. acnes in a patient comprises contacting a
CC   sample with a binding agent that binds to the proteins of the invention
CC   and determining the amount of bound protein in the sample. The
CC   polypeptides may be used as antigens in the production of antibodies
CC   specific for P. acnes proteins. These antibodies can be used to
CC   downregulate expression and activity of P. acnes polypeptides and
CC   therefore treat P. acnes infections. The antibodies may also be used as
CC   diagnostic agents for determining P. acnes presence, for example, by
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CC   enzyme linked immunosorbent assay (ELISA). Note: The sequence data for
CC   this patent did not form part of the printed specification, but was
CC   obtained in electronic format directly from WIPO at
CC   ftp.wipo.int/pub/published_pct_sequences
XX
SQ   Sequence 140 AA;

  Query Match             1.3%;  Score 9;  DB 4;  Length 140;
  Best Local Similarity   100.0%;  Pred. No. 7.1;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        107 STDSSATSS 115
              |||||||||
Db         90 STDSSATSS 98
```

". To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is an isolated hyper immune serum reactive hyper immune serum reactive antigen comprising the amino acid sequence of SEQ.ID.NO:32 structure/function of the product being claimed. There is not even identification of any particular portion of the structure that must be conserved in order to be "hyper immune serum reactive fragments ".

The instant specification may provide an adequate written description for an isolated hyper-immune serum reactive antigen *S.epidermidis* comprising the amino acid sequence set forth as SEQ ID NO. 32and is used together with an adjuvant for inducing a partial protective immune response. The specification fails to disclose isolated hyper immune serum reactive antigen comprising fragments thereof. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus 'fragments thereof"

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject

matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable .The instant specification may provide an adequate written description an isolated hyper immune serum reactive antigen SEQ.ID. NO: 32however, the specification fails to teach isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of isolated hyper

immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32as per Lilly by structurally describing a representative number of fragments or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus" have to disclosed. In this application such structural features common to the isolated hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32have not been disclosed. Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." In this case, the specification does not disclose isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32, required to practice the claims in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of hyper immune serum reactive antigen comprising fragments nor does the specification provide any partial structure of such isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32, nor any physical or chemical characteristics of the isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32nor any functional characteristics coupled with a known or disclosed hyper immune serum reactive antigen correlation between structure and function. Although the specification discloses an isolated hyper immune serum reactive antigen comprising the amino acid sequence SEQ.ID. NO: 32and does not provide a description of hyper immune serum reactive antigen comprising fragments that would satisfy the standard set out in Enzo.

The specification also fails to describe isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32by the test set out in Lilly. The specification describes only protein comprising the amino acid sequence SEQ.ID. NO: 32 that can be used as pharmaceutical composition against streptococcal infection caused by Streptococcus epidermidis using said hyper immune serum reactive antigen Therefore, it necessarily fails to describe a "representative number" of such species, isolated serum reactive hyper immune serum reactive antigen comprising undefined fragments of SEQ.ID. NO: 32. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Thus, the specification fails to teach the isolated serum reactive hyper immune serum reactive antigen

comprising undefined fragments of SEQ.ID. NO: 32and does not satisfy the written description guidelines.

Thus the claims do not comply with 35 USC 112, first paragraph because they are not supported by an adequate written description in the specification.

9. Claims 38-50, 53 and 54 are also rejected under 35 U.S.C. 112, first paragraph, , because the specification, while being enabling for an isolated hyper immune serum reactive *S.epidermidis* antigen comprising the amino acid sequence SEQ.ID. NO: 32o r an hyper immune serum reactive antigenic fragment consisting of amino acids of 6-28, ------ of SEQ ID NO. 32 and a pharmaceutical composition comprising the amino acid sequence SEQ.ID. NO: 32, pharmaceutically acceptable carrier does not reasonably provide enablement for a hyperimmune serum-reactive *S.epidermidis* antigen comprising fragment thereof , wherein the hyper immune serum reactive antigen comprises amino acids of 6-28----- of SEQ ID NO. 32 and a pharmaceutical composition comprising said hyper immune serum reactive antigen comprising fragment thereof , said pharmaceutical composition further comprising an immunostimulatory substance a peptide containing at least two Lys-Leu-Lys motifs, said composition is a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 38-50, 53 and 54 are drawn to a hyperimmune serum-reactive S.epidermidis hyper immune serum reactive antigen and pharmaceutical composition comprising an amino acid sequence of SEQ.ID.NO:32 or fragments thereof, said hyper immune serum reactive antigen or fragment comprising at least 6 or 8 or 10 contiguous amino acids of SEQ.ID.NO:32, said hyper immune serum reactive antigen or fragment comprising an amino acid sequence of 6-28, 54-59, 135-147, 193-205, 274-279, 284-291,298-308, 342-347, 360-366, 380-386, 408-425, 437-446, 457-464, 467-477, 504-510, 517-530, 535-543, 547-553, 562-569, 573-579, 592-600, 602-613, 626-631, 638-668 and/or 396-449 of SEQ ID NO: 32 , said pharmaceutical composition comprising t least one hyper immune serum reactive antigen or fragment and optionally a pharmaceutically-acceptable carrier or excipient, said composition further comprising an immunostimulatory substance, wherein the immunostimulatory substance is a peptide containing at least two Lys-Leu-Lys motifs and said pharmaceutical composition is a vaccine.

This means that the claims are drawn to a whole multitude of undefined hyperimmune serum fragments.

The instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The specification teaches that every human being is colonized with *S. epidermidis*. The normal habitats of *S. epidermidis* are the skin and the mucous membrane. Most frequently it causes surgical wound infections, and induces the formation of abscesses. The specification also teaches genomic DNA from *S. epidermidis* RP62A extracted and libraries were generated. The LSE-70 library in pMAL9.1 was screened with 10Dg biotinylated, human serum (PI5-IgG) in the first and second selection round. As negative control, no serum was added to the library cells for screening. Number of cells selected after the 1st and 2nd elution are shown for each selection round. Figure 3B shows the reactivity of specific clones (1-26) isolated by bacterial surface display as analysed by Western blot analysis with the human serum (PI5-IgG) used for selection by MACS at a dilution of 1:3,000. Table 1 shows Immunogenic proteins identified by bacterial surface display. A, LSE-70 library in lamB with PI5-IgG (804), B, LSE-150 library in fhuA with PI5-IgG (826), C, LSA-300 library in fhuA with PI5-IgG (729), prediction of antigenic sequences longer than 5 amino acids was performed with the program ANTIGENIC {Kolaskar, A. et al., 1990}. One such predicted sequence is SEQ.ID.NO:32 comprising 676 amino acid sequence . The specification hypothesizes that the polypeptide fragments are of use in pharmaceutical compostions etc .

One cannot extrapolate the teaching of the specification to the scope of the claims because the claims as broadly drawn include hyper immune serum reactive antigens comprising fragments and is acknowledged to be unpredictable because the specification fails to disclose the critical residues that are important for any function or disclose any changes made in an antigen, SEQ.ID.NO: 32 to obtain fragments that can be used for *S.epidermidis* infection. The claims as written are drawn to undefined polypeptides which comprise at least 5 or more contiguous amino acids of SEQ ID NO:32, wherein the three dimensional structure of

the amino acids comprised within the polypeptides are unknown and neither the specification nor the art of record define which amino acid residues of SEQ ID NO: 32 are critical as hyper immune serum reactive antigen . Bowie et al (Science, 1990, 257:1306-1310), teaches that an amino acid sequence encodes a message that determines the shape of a protein and determines the ability of said protein to fold into unique three-dimensional structures that allows them to function. Bowie further teaches that certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (p. 1306, cols 1 and 2). Clearly, the three dimension structure of a protein is critical to the production of antibodies given the teaching of Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pages 58-59). Herbert et al who specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. B cell epitopes on protein antigens are of variable size comprising up to about 20 amino acids. Antibodies bind in a more or less exact three dimensional fit with an epitope. This may be formed from residues on different regions of a protein antigen molecule which, in the native state, are closely apposed due to protein folding. Thus the three-dimensional structure of the protein molecule may be essential for antibody binding. (p. 58). However, neither the specification nor the art of record provide teachings that provide information about the residues critical for epitopes required for the establishment of an immune response that will produce antibodies that recognize full-length polypeptide, SEQ.ID.NO: 32. This information appears to be critical because the art recognizes (see Bowie above) that it is the protein sequence that determines the three dimensional shape of a protein and Herbert et al specifically state that antibodies bind in a more or less exact three dimensional fit and suggests that the three-dimensional structure of the protein molecule may be essential for antibody binding. Thus, in the absence of guidance in the specification and one could not determine how to make the claimed invention or predict that any particular linear peptide would function as claimed with a reasonable expectation of success. Neither the art nor the specification as originally filed provides guidance on how to determine which 15 or 20 amino acids will be capable of, when used as an immunogen, raising antibodies which bind specifically to SEQ ID NO:32. In particular, Roitt et al (Immunology, 1993, Mosby, St. Louis, p 7.7-7.8) teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions.

These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability' (p. 513, col 1). Furthermore, the specification does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation. Given this teaching, even if the claimed peptides consists of amino acid residues that were 100% identical to portions of SEQ ID NO:32 it would not be possible to determine with any predictability whether the antibodies produced from said peptide would be for SEQ ID NO:32 and actually bind to SEQ ID NO: 32 in the absence of guidance from the specification. It is obvious that t cell epitopes and antibody epitopes are not the same. However, the issues drawn to the lack of guidance in the specification as to critical residues and polypeptide fragments required for T cell binding are relevant to this limitation as well. Further, there is no teaching in the specification of whether or not the epitopes are linear or comprise 3-dimensional structures. In particular, Greenspan et al (Nature Biotechnology, 1999, 7:936-937) teaches that defining epitopes is not as easy as it seems. Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column).

As drawn specifically to fragments of SEQ ID NO: 32, Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach that a single amino acid changes in an antigen can effectively abolish antibody antigen binding. Furthermore, Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444, see abstract in particular) teach single amino acid substitutions outside the antigenic site on a protein affects antibody binding. Clearly if antibody binding is abolished, it is because of the alteration of the conformation of the epitope to which the antibody binds. Given the clear teaching drawn to conformation alteration with even a single amino acid change, clearly it would be expected that amino acid residues outside of the

antigenic epitope, not native to SEQ ID NO: 32 would alter the conformation of that epitope in the polypeptide comprising and that it could not be predicted, nor would it be expected that a structurally altered antigenic epitope would produce, for example, antibodies that would bind to SEQ ID NO: 32.

The specification provides no guidance or working examples which would provide guidance to one skilled in the art as to which amino acids or polypeptide fragments are critical as hyperimmune serum reactive antigen and are specific for SEQ ID NO: 32 and no evidence has been provided which would allow one of skill in the art to predict which of the broadly claimed polypeptide fragments/variants would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

Thus, it would not be expected that the claimed fragments/variants in the absence of further guidance from the specification, would function as claimed or as contemplated given that there is no teaching of residues critical to the claimed function. Further one would not know how to use of said variants that induce response and do not bind to the full length SEQ ID NO:32.

Claim objections/ Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

MPEP: 2173 states that claims must particularly point out and distinctly claim the Invention.

The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention. In claim 39, table 1

contains several sequences and there is no practical way of defining the invention clearly.

Claim Objections

12. Claim 38 is objected because it recites non elected sequences ,SEQ.ID.NO 33-62 as the elected invention is SEQ.ID.NO:32.

Claim Rejections - 35 USC 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

14. Claims 38-44, 45-49 and 53-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Kimmerly WJ , AAG81977 , WO200134809-A2 (As this document contains more than 2189 pages, the examiner is not sending the patent and therefore, attached the sequence alignment with abstract)

Claims are drawn to a pharmaceutical composition comprising at least one hyper immune serum reactive antigen *S.epidermidis* hyper immune serum reactive antigen SEQ ID NO. 32 or fragments thereof and optionally a pharmaceutically-acceptable carrier or excipient said pharmaceutical composition further comprising an immunostimulatory substance.

Kimmerly WJ disclose an antigen comprising (i.e., fragment) fragment and said fragment is 52.4% identical to the claimed hyper immune serum reactive antigen *S.epidermidis* antigen comprising fragments thereof (see the sequence alignment). As the polypeptide binds to serum antibodies it reads on hyper immune serum antigen. Thus the prior art read on the claims 38-44 . The teaching of the Kimmerly WJ disclose that the pharmaceutical compositions comprise therapeutic amount of peptide fragments (---) in a pharmaceutically acceptable carrier

(pages 33-35 of patent).) and thus it reads on claims 45-46. The same compositions comprises two different hyper immune serum reactive antigen as 356 amino acid sequence comprises different fragments and thus read on claims 47 and 48 . This composition is a vaccine composition as it used for therapeutic or preventive disease and thus meet the limitations of claim 53-54 (pages 33-35 of patent). Further, the art reads on claim 49 as the composition comprise immunostimulatory substance such as adjuvants etc (pages 33-35 of patent. Thus, the prior art anticipated the claimed invention.

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AG81977
ID   AAG81977 standard; protein; 356 AA.
XX
AC   AAG81977;
XX
DT   03-SEP-2001  (first entry)
XX
DE   S. epidermidis open reading frame protein sequence SEQ ID NO:1048.
XX
KW   Staphylococcus epidermidis SR1 strain; infection; diagnosis; vaccination;
KW   endocarditis.
XX
OS   Staphylococcus epidermidis.
XX
PN   WO200134809-A2.
XX
PD   17-MAY-2001.
XX
PF   09-NOV-2000; 2000WO-US030782.
XX
PR   09-NOV-1999;   99US-0164258P.
XX
PA   (GLAX ) GLAXO GROUP LTD.
XX
PI   Kimmerly WJ;
XX
DR   WPI; 2001-316495/33.
DR   N-PSDB; AAH52827.
XX
PT   Nucleic acids encoding polypeptides from Staphylococcus epidermidis,
PT   useful for vaccinating against infections, e.g. endocarditis.
XX
PS   Claim 18; Page 305; 2188pp; English.
XX
CC   AAH52304 to AAH53970 represent nucleic acids (I) encoding polypeptides
CC   (II), given in AAG81454 to AAG83120, from Staphylococcus epidermidis. (I)
CC   and (II) can have antibacterial activity and therefore can be used in
CC   vaccination. The nucleic acids (I) may be used to produce the S.
CC   epidermidis polypeptides (II) via the production of vectors containing
CC   them which are used to produce hosts cells which express the
CC   polypeptides. The polypeptides (II) (and/or nucleic acids) may then be
CC   used to vaccinate subjects and to raise antibodies against the bacteria.
CC   The polypeptides may also be used to assay for other inhibitors of their
CC   activity and therefore identify compounds that may be used for the
CC   treatment of S. epidermidis infections, e.g. endocarditis. AAH53971 to
CC   AAH55090 represent specifically claimed S. epidermidis genomic DNA
CC   polynucleotide sequences from the present invention. AAH55091 to AAH55098
CC   represent oligonucleotide sequences and primers which are used in the
CC   exemplification of the present invention. N.B. The present invention
CC   specifically claims all the polynucleotide sequences given in the
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CC   sequence listing of the present specification, however the sequence
CC   listing only goes up to SEQ ID NO:4454 so even though sequences are given
CC   in the disclosure for SEQ ID NO:4465 to 4472, no sequences are present
CC   for SEQ ID NO:4455 to 4464
XX
SQ   Sequence 356 AA;

  Query Match             52.4%;  Score 1765;  DB 4;  Length 356;
  Best Local Similarity   100.0%;  Pred. No. 1.7e-87;
  Matches  356;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        321 MNLRSLDTKVEDNNTLSDDKKQALKQEIDKTKQSIDRQRNIIIDQLNGASNKKQATEDIL 380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MNLRSLDTKVEDNNTLSDDKKQALKQEIDKTKQSIDRQRNIIIDQLNGASNKKQATEDIL 60

Qy        381 NSVFSKNEVEDIMKRIKTNGRSNEDIANQIAKQIDGLALTSSDDILKSMLDQSKDKESLI 440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 NSVFSKNEVEDIMKRIKTNGRSNEDIANQIAKQIDGLALTSSDDILKSMLDQSKDKESLI 120

Qy        441 KQLLTTRLGNDEADRIAKKLLSQNLSNSQIVEQLKRHFNSQGTATADDILNGVINDAKDK 500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 KQLLTTRLGNDEADRIAKKLLSQNLSNSQIVEQLKRHFNSQGTATADDILNGVINDAKDK 180

Qy        501 RQAIETILQTRINKDKAKIIADVIARVQKDKSDIMDLIHSAIEGKANDLLDIEKRAKQAK 560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 RQAIETILQTRINKDKAKIIADVIARVQKDKSDIMDLIHSAIEGKANDLLDIEKRAKQAK 240

Qy        561 KDLEYILDPIKNRPSLLDRINKGVGDSNSIFDRPSLLDKLHSRGSILDKLDHSAPENGLS 620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KDLEYILDPIKNRPSLLDRINKGVGDSNSIFDRPSLLDKLHSRGSILDKLDHSAPENGLS 300

Qy        621 LDNKGGLLSDLFDDDGNISLPATGEVIKQHWIPVAVVLMSLGGALIFMARRKKHQN 676
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 LDNKGGLLSDLFDDDGNISLPATGEVIKQHWIPVAVVLMSLGGALIFMARRKKHQN 356
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15. Claims 38-44, 45-49 and 53-54 are rejected under 35 U.S.C. 102(e) as being anticipated by Doucette-Stamm et al Patent No. 6380370.

Claims are drawn to a pharmaceutical composition comprising at least one hyper immune serum reactive antigen *S.epidermidis* hyper immune serum reactive antigen SEQ ID NO. 32 and optionally a pharmaceutically-acceptable carrier or excipient said pharmaceutical composition further comprising an immunostimulatory substance.

Doucette-Stamm et al disclose an isolated hyper immune serum reactive antigen comprising the amino acid sequence SEQ.ID.NO;4318 (i.e., fragment) and is 98.7 % identical to the claimed SEQ.ID.NO: 32 (see the sequence alignment).

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US-09-134-001C-4318
; Sequence 4318, Application US/09134001C
; Patent No. 6380370
; GENERAL INFORMATION:
;  APPLICANT: Lynn Doucette-Stamm et al
;  TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO STAPHYLOCOCCUS
;  TITLE OF INVENTION:  EPIDERMIDIS FOR DIAGNOSTICS AND THERAPEUTICS
;  FILE REFERENCE: GTC-007
;  CURRENT APPLICATION NUMBER: US/09/134,001C
;  CURRENT FILING DATE:  1998-08-13
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;  PRIOR APPLICATION NUMBER: US 60/064,964
;  PRIOR FILING DATE: 1997-11-08
;  PRIOR APPLICATION NUMBER: US 60/055,779
;  PRIOR FILING DATE: 1997-08-14
;  NUMBER OF SEQ ID NOS: 5674
; SEQ ID NO 4318
;   LENGTH: 676
;   TYPE: PRT
;   ORGANISM: Staphylococcus epidermidis
US-09-134-001C-4318

  Query Match             98.7%;  Score 3325;  DB 2;  Length 676;
  Best Local Similarity   99.0%;  Pred. No. 1e-214;
  Matches  669;  Conservative    0;  Mismatches    7;  Indels    0;  Gaps    0;

Qy          1 MKRTDKIGVYLKLSCSALLLSGSLVGYGFTKDAFADSESTSSNVENTSNSNSIADKIQQA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKRTDKIGVYLKLSCSALLLSGSLVGYGFTKDAFADSESTSSNVENTSNSNSIADKIQQA 60

Qy         61 KDDIKDLKELSDADIKSFEERLDKVDNQSSIDRIINDAKDKNNHLKSTDSSATSSKTEDD 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 KDDIKDLKELSDADIKSFEERLDKVDNQSSIDRIINDAKDKNNHLKSTDSSATSSKTEDD 120

Qy        121 DTSEKDNDDMTKDLDKILSDLDSIAKNVDNRQQGEERASKPSDSTTDEKDDSNNKVHDTN 180
              ||||||||||||||||||||||||||||||||||  ||||||||||||||||||||||||
Db        121 DTSEKDNDDMTKDLDKILSDLDSIAKNVDNRQQGENSASKPSDSTTDEKDDSNNKVHDTN 180

Qy        181 ASTRNATTDDSEESVIDKLDKIQQDFKSDSNNNPSEQSDQQASPSNKTENNKEESSTTTN 240
              ||||||||||||||||||||||||||||||  ||||||||||||| ||||||||||||
Db        181 ASTRNATTDDSEESVIDKLDKIQQDFKSDSNNKLSEQSDQQASPSNKNENNKEESSTTTN 240

Qy        241 QSDSDSKDDKSNDGHRSTLERIASDTDQIRDSKDQHVTDEKQDIQAITRSLQGSDKIEKA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 QSDSDSKDDKSNDGRRSTLERIASDTDQIRDSKDQHVTDEKQDIQAITRSLQGSDKIEKA 300

Qy        301 LAKVQSDNQSLDSNYINNKLMNLRSLDTKVEDNNTLSDDKKQALKQEIDKTKQSIDRQRN 360
              |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 LAKVQSDNQPLDSNYINNKLMNLRSLDTKVEDNNTLSDDKKQALKQEIDKTKQSIDRQRN 360

Qy        361 IIIDQLNGASNKKQATEDILNSVFSKNEVEDIMKRIKTNGRSNEDIANQIAKQIDGLALT 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 IIIDQLNGASNKKQATEDILNSVFSKNEVEDIMKRIKTNGRSNEDIANQIAKQIDGLALT 420

Qy        421 SSDDILKSMLDQSKDKESLIKQLLTTRLGNDEADRIAKKLLSQNLSNSQIVEQLKRHFNS 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 SSDDILKSMLDQSKDKESLIKQLLTTRLGNDEADRIAKKLLSQNLSNSQIVEQLKRHFNS 480

Qy        481 QGTATADDILNGVINDAKDKRQAIETILQTRINKDKAKIIADVIARVQKDKSDIMDLIHS 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 QGTATADDILNGVINDAKDKRQAIETILQTRINKDKAKIIADVIARVQKDKSDIMDLIHS 540

Qy        541 AIEGKANDLLDIEKRAKQAKKDLEYILDPIKNRPSLLDRINKGVGDSNSIFDRPSLLDKL 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 AIEGKANDLLDIEKRAKQAKKDLEYILDPIKNRPSLLDRINKGVGDSNSIFDRPSLLDKL 600

Qy        601 HSRGSILDKLDHSAPENGLSLDNKGGLLSDLFDDDGNISLPATGEVIKQHWIPVAVVLMS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 HSRGSILDKLDHSAPENGLSLDNKGGLLSDLFDDDGNISLPATGEVIKQHWIPVAVVLMS 660

Qy        661 LGGALIFMARRKKHQN 676
              ||||||||||||||||
Db        661 LGGALIFMARRKKHQN 676
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The disclosed antigen is reactive to serum antibodies (see column 40) and therefore,it is hyper immune serum reactive antigen . Thus the prior art read on the claims 38-44 drawn to fragments ranging from 5 or more amino acids . The teaching of the Patent No. 6380370

disclose that the pharmaceutical compositions comprise therapeutic amount of peptide SEQ.ID.NO: 4318 (see columns 37 –38) in a pharmaceutically acceptable carrier and thus read on claims 45-46. The same compositions comprises two different hyper immune serum reactive antigen as 676 amino acid sequence comprises different fragments and thus read on claims 47 and 48 . This composition is a vaccine composition as it used for therapeutic or preventive disease and thus meet the limitations of claim 53-54. Further, the art reads on claim 49 as the composition comprise immunostimulatory substance such as adjuvants etc(see columns 37 –38). Thus, the prior art anticipated the claimed invention.

Remarks

16. No claims are allowed.

Relevant Prior Art

17. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600 or Art Unit 1645 LIE, Victor Barlow whose telephone number is 571-272-0506.

Padma Baskar Ph.D

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER